

Amendments to Claims:

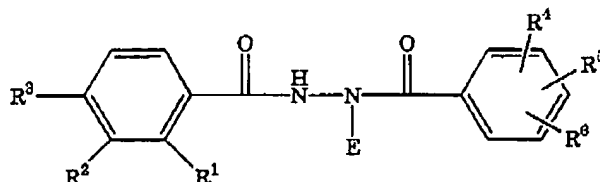
This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (cancelled)

Claim 2 (cancelled)

Claim 3 (previously presented) A method to modulate the expression of one or more exogenous genes in a subject, wherein the subject is other than a plant, comprising administering to the subject an effective amount of a ligand of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R^4 , R^5 , and R^6 are independently H, Me, Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;

provided that:

- a) when R^1 is Me and R^2 is OMe;
then R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R^1 is Me and R^2 is OEt;
then R^3 is H and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;
- c) when R^1 is Et and R^2 is OMe or OEt;
then R^3 is H and the combination R^4 , R^5 , and R^6 is:
 - i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
 - ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;
- d) when R^1 is i-Pr;
then R^2 is OMe, or OEt; R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- e) when R^3 is Et;
then R^2 is H, R^1 is F or Cl, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
then R^1 is Me or Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;
then R^1 is Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- h) when R^1 is formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN, or $SCHF_2$;

then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and

- i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;

then R¹ is Et, R³ is H, the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

wherein the cells of the subject contain:

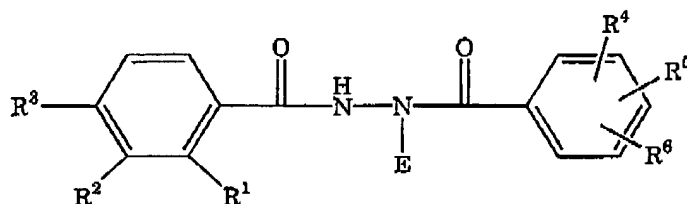
- a) an ecdysone receptor complex comprising:
 - 1) a DNA binding domain;
 - 2) a binding domain for the ligand; and
 - 3) a transactivation domain; and
- b) a DNA construct comprising:
 - 1) the exogenous gene; and
 - 2) a response element; and

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene.

Claim 4 (original) A method for producing a polypeptide comprising the steps of:

- a) selecting a cell which is substantially insensitive to exposure to a ligand of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

- R^1 is H, Me, Et, i-Pr, F, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN, or $SCHF_2$;
- R^2 is H, Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, $SOCF_3$, OCF_2CF_2H , COEt, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, OCF_3 , $OCHF_2$, O-i-Pr, SCN, $SCHF_2$, SMe, NH-CN, or joined with R^3 and the phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;
- R^3 is H, Et, or joined with R^2 and the phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;
- R^4 , R^5 , and R^6 are independently H, Me, Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, CCH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

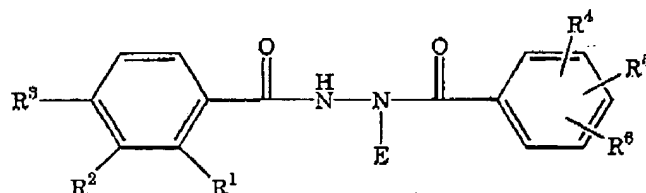
provided that:

- a) when R^1 is Me and R^2 is OMe;
then R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R^1 is Me and R^2 is OEt;
then R^3 is H and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;
- c) when R^1 is Et and R^2 is OMe or OEt;
then R^3 is H and the combination R^4 , R^5 , and R^6 is:
 - i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
 - ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

- d) when R^1 is i-Pr;
then R^2 is OMe, or OEt; R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
 - e) when R^3 is Et;
then R^2 is H, R^1 is F or Cl, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
 - f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
then R^1 is Me or Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
 - g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;
then R^1 is Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
 - h) when R^1 is formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN , $C=CH$, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN , or $SCHF_2$;
then R^2 is OMe or OEt, R^3 is H, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me; and
 - i) when R^2 is Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN , $C=CH$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe_2 , NEt_2 , SMe, SEt, $SOCF_3$, OCF_2CF_2H , COEt, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, OCF_3 , $OCHF_2$, O-i-Pr, SCN , $SCHF_2$, $SOMe$, or $NH-CN$;
then R^1 is Et, R^3 is H, the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- b) introducing into the cell:
- 1) a DNA construct comprising:
 - a) an exogenous gene encoding the polypeptide; and
 - b) a response element;wherein the gene is under the control of the response element; and
 - 2) an ecdysone receptor complex comprising:
 - a) a DNA binding domain;
 - b) a binding domain for the ligand; and
 - c) a transactivation domain; and

c) exposing the cell to the ligand.

Claim 5 (previously presented) A method for regulating endogenous or heterologous gene expression in a transgenic organism, wherein the organism is other than plant, comprising contacting a ligand of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SET, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;

provided that:

a) when R¹ is Me and R² is OMe;

- then R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R^1 is Me and R^2 is OEt;
then R^3 is H and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;
- c) when R^1 is Et and R^2 is OMe or OEt;
then R^3 is H and the combination R^4 , R^5 , and R^6 is:
i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when R^1 is i-Pr;
then R^2 is OMe, or OEt; R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- e) when R^3 is Et;
then R^2 is H, R^1 is F or Cl, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
then R^1 is Me or Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;
then R^1 is Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- h) when R^1 is formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN, or $SCHF_2$;
then R^2 is OMe or OEt, R^3 is H, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me; and
- i) when R^2 is Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, $SOCF_3$, OCF_2CF_2H ,

COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SMe, or NH-CN;

then R¹ is Et, R³ is H, the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

with an ecdysone receptor complex within the cells of the organism wherein the cells further contain a DNA binding sequence for the ecdysone receptor complex when in combination with the ligand and wherein formation of an ecdysone receptor complex-ligand-DNA binding sequence complex induces expression of the gene.

Claim 6 (cancelled)

Claim 7 (original) The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.

Claim 8 (original) The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.

Claim 9 (original) The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.

Claim 10 (cancelled)

Claim 11 (original) The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.

Claim 12 (original) The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.

Claim 13 (original) The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.

Claim 14 (cancelled)

Claim 15 (original) The method of Claim 3 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

Claim 16 (original) The method of Claim 4 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

Claim 17 (original) The method of Claim 5 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

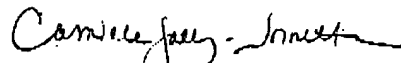
Claim 18 (cancelled)

Claim 19 (original) The method of Claim 3 wherein the subject is a mammal.

Claim 20 (previously presented) The method of Claim 3 wherein the subject is a fungus or yeast.

In view of the foregoing amendments, Applicants submit that the
"Amendments to the Claims" is in compliance with 37 CFR § 1.121.

Respectfully submitted,


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